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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Masashi Ito

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EXAMINER

SAJJADI, FEREDYDOUN GHOTB

ART UNIT

PAPER NUMBER

1633

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/518,472	Applicant(s) ITO ET AL.	
	Examiner FEREYDOUN G. SAJJADI	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-11 and 17-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-11 and 17-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/26/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response of December 14, 2009, to the non-final action dated June 16, 2009, has been entered. Claim 3 has been cancelled. No claims were amended or newly added. Accordingly, claims 1, 2, 4-11 and 17-19 remain pending in the Application and are under current examination. The claims have been examined commensurate in scope with the elected species of insulin genes as the foreign DNA encoding a secreted protein.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on February 26, 2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner, and indicated as such on IDS form PTO-SB/08A.

Withdrawn Claim Rejections - 35 USC § 112- Second Paragraph

Claim 3 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the previous Office action dated June 16, 2009. Applicants have cancelled the claim, rendering its rejection moot. Thus, the rejection is hereby withdrawn.

Response & Maintained Claim Rejections - 35 USC § 103

Claim 1, 2, 4-11, and 17-19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Darimont et al. (WO 02/06450; Publication date: 24, January 2002), in view of Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999). Applicants' cancellation of claim 3 renders its rejection moot. The rejection set forth on pp. 4-6 of the previous Office action dated June 16, 2009 is maintained for reasons of record.

The rejection:

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The claims are directed to a population of primary cultured preadipocytes, wherein the preadipocytes stably maintain a foreign DNA encoding secreted insulin gene, operably linked to a promoter.

Darimont et al. describe the establishment of human preadipose cell lines capable of differentiating to adipose cells for development of drugs against obesity, diabetes and cardiovascular disease (Abstract). The isolation from subcutaneous adipose tissue and the primary culture of preadipose cells by “ceiling culture method” is described on p. 7, Example 1, and p. 5, lines 20-29 and Fig. 1. The de-differentiation of adipocytes to preadipocytes is described in Example 2, p. 8. Darimont et al. further describe the immortalization of the cells by introducing and stably expressing the SV40 large T antigen via a retroviral vector (Example 3, p. 8).

While Darimont et al. do not describe the expression of a foreign insulin gene in the preadipocyte cell, such was known in the prior art. Furcht et al. teach multipotent adult stem cells that can be maintained in culture in the undifferentiated state, or differentiated to form cells of multiple tissue types, as well as methods for producing the same, for therapeutic use (Abstract). The isolation of the bone marrow derived mononuclear cells is described in Example 1 (column 44), and their differentiation into adipocytes is outlined in Example 2 (column 46). The bone marrow derived stem cells are also referred to as mesenchymal stem cells and marrow stromal cells (column 49). Adipocytes derived from the stem cells can be used for the treatment of Type II diabetes (column 25). Furcht et al. describe a number of secreted genes that may be used for gene therapy of diabetes (column 30). Additionally described are viral transfer vectors, including retroviruses (column 32). Retroviral vectors are extensively described in column 35. Following *in vitro* culture and gene transfer, the transfected cells may be introduced locally or infused systemically (column 30). Specific examples of engraftment by intramuscular injection or stereotaxic transplantation into mice are described in Example 10 (columns 54-55). Furcht et al. describe the use of their adipocytes for implantation in reconstructive surgery, as well as treatment of Type II diabetes (column 25, lines 50-52), in addition to the encapsulation of genetically altered cells for delivery into a patient to produce insulin (paragraph 31, lines 35-64). Furcht et al. further teach that the genetically altered stem cells can also be encapsulated in an

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inert carrier to allow the cells to be protected from the host immune system while producing the secreted protein (column 31). A number of pharmaceutically acceptable inert carriers materials, that include polymers and capsules are described in column 31. The introduction of the cells into the body of a subject in conjunction with a suitable matrix implant or polymer capsule is described in column 8, lines 8-14). With specific reference to treatment for diabetes, the authors state that autologous stem cells that have been genetically altered with a retroviral vector to produce insulin at physiologically therapeutic levels can be encapsulated for delivery within the patient's tissues, to produce insulin for extended periods of time (column 31). Furcht et al. further describe stem cells transfected with factor IX, that secrete the protein for at least 8 weeks after infusion into mice (column 30).

The inventions of both Darimont et al. and Furcht et al. are both directed to the transfection and differentiation of cells into adipocytes. Therefore, a person of ordinary skill in the art would have been motivated to combine their respective teachings and substitute primary cultured preadipocytes for stromal cell preadipocytes as a matter of design choice, and to forego the isolation and differentiation of stromal or mesenchymal stem cells. A person of ordinary skill in the art, having introduced an insulin gene by the expression vector of Furcht et al., to the primary cultured preadipocytes of Darimont et al. would be able to practice the instantly claimed method of the invention, with a reasonable expectation of success. Thus it would have been *prima facie* obvious for a person of ordinary skill in the art, to introduce an insulin gene and an angiogenesis factor to preadipocytes, at the time of the instant invention.

Response to Arguments:

Applicants traverse the rejection, arguing that the present invention is directed to a population of primary cultured preadipocytes that are not immortalized cell lines or a cell population that has been manipulated to have enhanced replicative potential, whereas Darimont discloses the provision of human adipose cell lines that are further immortalized. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it is noted that Applicants' reading of Darimont et al. is incomplete and therefore ignores an analysis as a whole. As an initial matter, it should be noted that the instantly

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claimed primary cultured preadipocytes of base claim 1 have been manipulated to stably maintain any foreign DNA encoding a protein that is secreted, and thus have been manipulated. Further, Example 2 of Darimont et al. specifically describes the ceiling culture of primary adipocytes (limitation of instant claim 19) that spontaneously de-differentiate into preadipocytes (p. 8, lines 8-9). Thus, the preadipocytes of Darimont et al. read on any population of primary cultured preadipocytes.

With respect to immortalized cell lines, such is taught in Example 3, wherein the primary human de-differentiated preadipocytes obtained according to Example 2 are transfected with retroviral vector carrying the SV40 large T antigen (pp. 8-9). Thus, applicants have mischaracterized the teachings of Darimont et al. in their selective analysis.

Applicants next cite Kirkland et al. as teaching away from the present invention. Such argument is misplaced as Kirkland et al. has not been relied upon in the instant obviousness rejection (as acknowledged by Applicants). Arguments regarding Kirkland et al. are not on point and have thus not been further addressed.

Applicants next cite the prior art of Bestor et al. and Wei et al., arguing that even if retroviral vectors and adeno-associated viral vectors were known as vectors to achieve good expression of a foreign gene, long-term expression (such as for one year or more) of a foreign gene *in vivo* was against the technical common knowledge at the time of filing the present application. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., long-term expression of one year or more) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants additionally argue that at the time of filing of the present application knowledge about the life span and renewal of adipose cells in a body was scarce and that Applicants have shown surprising and unexpected results. Such is not found persuasive, because the longevity or half-life of adipocytes in a living body is irrelevant to the instantly claimed composition or its' method of production. As stated in MPEP 2143.02, obviousness requires only a reasonable expectation of success.

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With regards to Applicants' arguments that the preadipocytes have various advantageous characteristics not suggested by the cited references, it should be noted that such characteristics are an inherent property of the adipocytes and thus necessarily present. Moreover, "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). "It is not invention to perceive that the product which others had discovered had qualities they failed to detect." *Gen. Elec. Co. v. Jewel Incandescent Lamp Co.*, 326 U.S. 242, 249 (1945).

Thus, the rejection is maintained for reasons of record and the preceding commentary.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREDYOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Primary Examiner, Art Unit 1633